Limb Graft Occlusion Following EVAR: Clinical Pattern, Outcomes and Predictive Factors of Occurrence

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Introduction. We reviewed our experience with limb occlusion after EVAR in order (1) to assess the clinical pattern and treatment options (2) to assess outcomes and (3) to identify predictive factors of occurrence.

Materials and method. Between 1995 and 2005, 460 AAA patients were electively treated with a variety of commercially available stent grafts. There were 369 bifurcated and 91 aortouniiliac grafts (829 limbs). Follow-up included physical examination, plain X-ray, Duplex ultrasonography, and spiral computed tomographic scans at 1, 6, 12 months and annually thereafter. All pertinent data were collected prospectively and analysed retrospectively. The follow-up period ranged from Day 0 to 104 months, with a median follow-up of 23.4 months.

Results. 36 limbs in 33 patients (7.2%) occluded between Day 0 and 71 months (average: 9.5 months) after EVAR. Presentation was acute ischemia in 11 cases, rest pain in 9, claudication in ten. Four occlusions remained asymptomatic and two occurred intraoperatively. Treatment was femoro-femoral cross-over graft in 19 cases, axillo-femoral bypass in three, thrombectomy and stent in three, thrombolysis and stent in nine, and conservative in two. One patient (3%) died of multiple organ failure after thrombolysis. There was no amputation. Reocclusions occurred in two patients (6.1%). Multivariate logistic regression showed that kinking (odds ratio [OR] 11.9; confidence interval [CI] 3.39–42.1; \( p = 0.0001 \)), first graft generation (OR 2.87; CI 1.25–6.62; \( p = 0.017 \)) and younger age (OR 1.05; CI 1.00–1.09; \( p = 0.034 \)) were independently related to the occurrence of graft limb occlusion.

Conclusion. Acute graft limb occlusion is not rare after EVAR. The frequency of limb occlusion has declined with current stent grafts generation. Although surgery and endovascular treatments are efficient and safe, development of a graft limb kink should lead to aggressive pre-emptive treatment to prevent occlusion.

Keywords: Abdominal aortic aneurysm; Endovascular grafting; Graft limb occlusion; Complications; Thrombolysis; Extra-anatomic bypass.

Introduction

Lower extremity ischemia is a known adverse event following endovascular abdominal aortic aneurysm repair (EVAR). Limb occlusion, embolism or access related problems\(^1\) are the main causes. So far, few studies\(^2\)–\(^4\) have specifically investigated this complication and studied the predictive factors.

We report herein our ten year experience with graft limb occlusion which occurred in patients who underwent EVAR in our institution.

The main objectives of this study were (1) to describe the clinical pattern and treatment options (2) to assess outcomes and (3) to identify predictive factors that could contribute to the occurrence of graft limb occlusion.

Methods

Between January 1995 and November 2005, 460 patients underwent endovascular treatment of an infrarenal abdominal aortic aneurysm in the department of vascular surgery of Henri Mondor Hospital. Clinical and anatomical data, operative managements and outcomes were collected prospectively and analysed retrospectively. For the purpose of this study we...
excluded from the analysis three patients who required acute conversion following failed EVAR deployment. Commercially available devices were used during this period. It included 310 Zenith, 60 Vanguard, 31 Gore, 21 AneurX, 14 EVT, 9 Stenford, 8 Stentor and 7 Talent. There were 369 bifurcated devices and 91 aortomonoiliac devices combined with femorofemoral bypass grafts, yielding a population of 829 limbs at risk for occlusion.

Endovascular grafts were deployed below the renal arteries in 145 cases and across the renal arteries in the remaining 315 cases. Distally limbs were deployed either in the common iliac artery or in external iliac artery, depending on the extent of the aneurysm. Following graft deployment, the entire length of the grafts was modelled with balloon dilatation. At the end of the procedure, control angiography was performed to assess proper graft function. Great care was taken to treat any severe kinks or stenosis which led in some instances to additional bare stent placement.

Post-operatively patients were prescribed anti-platelets in routine. Five per cent of them were taking Coumadin, the indication of which was arrhythmia or cardiac disorders. At one month, six months, 12 months and annually thereafter, patients were systematically reviewed for physical examination, plain X-ray, duplex ultrasonography, spiral computed tomographic scans. When clinical symptoms suggested endograft thrombosis, CT scan or angiography and duplex scans were obtained.

Patients with limb graft occlusion recognized by Duplex scan, CT-scan or arteriogram constitute the basis of the current study. They were compared to the group of patients who did not experience occlusion of graft limbs. Analysis was carried out on: (a) patient’s pre-operative data: age, gender, smoking, dyslipidemia, cardiac past history, renal insufficiency, hypertension, clinical presentation, (b) aneurysm features: diameter and angulation of the iliac arteries measured on intra-operative angiography, outflow, presence of thrombus in the infra renal aortic neck (c) stent graft used: configuration (bifurcated or aortouniiliac), type of device, extension of the limb of the graft to the external iliac artery, (d) grafts surveillance events during follow-up: migration, limb kinking.

Poor outflow was defined as a stenosis or an occlusion distal to the extremity of the limb of the graft identified on Duplex scan or CT-scan. Only common femoral or external iliac artery lesions were considered for the analysis.

Migration was defined as a displacement of the graft of at least one centimetre on CT-scan examination as compared to the first post-operative CT-scan. Kink was defined as a sharp localized angulation $>90^\circ$ of one or both limbs of the graft on plain X-ray examination.

Statistics

Results were expressed as percentages, mean ± 1 standard deviation or median, depending on variable distribution. Patients were considered as the unit of analysis for clinical data analysis; limbs were the unit of analysis for anatomical data analysis. For comparison, categorical variables were analysed using chi square test or Fisher’s exact test when appropriate. Continuous variables were analysed using Student’s t test or non parametric Mann Whitney test when appropriate. Statistically significant variables ($p < .05$) identified in the univariate analysis were further assessed by a multivariate logistic regression. The Kaplan-Meier method was used to estimate time to occurrence graft limb occlusion. Most significant factors were compared with means of log-rank test. All tests were 2-tailed and considered significant for $p \leq 0.05$.

Results

The series included 460 patients, 25 women (5.4%) and 435 men (94.6%), with a mean age of 72.3 ± 8 years (range, 47–88 years). All grafts were successfully deployed. The follow-up period ranged from day 0 to 104 months, with a mean follow-up of 28 months (median: 23.4 months). Median follow-up was 26.2 month for patients with graft limb occlusion and 22.3 for patients without graft limb thrombosis. During follow-up, 25 patients (5%) were lost to follow-up before the end of the study and 18 (4%) had died.

Thirty-six limbs in 33/460 (7.2%) patients occluded at some time during follow-up.

Clinical pattern and treatment options

Limb thrombosis was unilateral in 30 patients (91%) and bilateral in three (9%). Median time to occlusion was 1.4 months ranging from Day 0 to 71 months. Two patients (6.1%) occluded their grafts intra operatively, 9 (27.3%) within the first week, 14 (42.4%) within the first month, 23 (69.7%) within the first six months and 30 (90.9%) within the first 3 years (Fig. 1).
Excluding the two patients who occluded their graft intraoperatively, presenting symptoms were as follows: nine patients (27%) presented with acute ischemia, eight (24%) with rest pain and ten (30%) with claudication. In four patients (12%), the limb occlusions were asymptomatic and were found on systematic duplex-scan.

Treatment options are listed in Table 1. Whenever feasible an endovascular option was chosen first. Catheter directed intra arterial thrombolysis was chosen for patients with recent occlusion (<14 days), and no general contra-indication was present. After brachial puncture, the catheter was introduced from the arm and pushed into the thrombus. Thrombolysis was continued until the clots were cleared, for a maximum of 48 h. Any underlying causes were then treated which included stent placement. Surgery (including mechanical thrombectomy and extra-anatomic bypass) was performed in all other situations.

Outcomes

Out of the thirty-three patients who occluded, 32 (97%) survived. The remaining patient died (3%). This patient with a poor cardiac and pulmonary function was treated by EVAR for a >7 cm large asymptomatic aneurysm. After a few months, he presented with a bilateral acute ischemia of the lower extremities and an occluded graft. Intra-arterial thrombolysis restored the flow but the patient died of multiple organ failure four days afterwards.

After treatment, all alive patients cleared their symptoms without any lasting sequelae. However, three of these patients (9.4%) required a second re-intervention. Two patients (6.2%) experienced graft limb reocclusion. These two patients had been initially treated with thrombolysis + stenting. Reintervention consisted in a successfully iterative thrombolysis + stenting of the occluded limb in one and explantation of the endograft with aortobifemoral bypass in the second case. The third patient developed a sepsis of the groin. This patient had been treated with a femoro-femoral graft and needed a new femoro-femoral graft using a cryopreserved allograft. He was still alive at the completion of the study. No patient was amputated.

The two patients treated conservatively remained asymptomatic with a follow-up period of three and seven years respectively.

In summary 32/33 (97%) patients survived symptom free and 29/33 (87.9%) experienced an uneventful outcome after reoperation.

Analysis of predictive factors of thrombosis

Patient’s related factors

Patients who developed graft limb thrombosis were significantly younger as compared with patients without graft limb occlusion (mean age: 68.5 versus 72.6; $p = .007$). For remaining factors, statistical analysis failed to show a significant association between limb thrombosis and gender, current smoking, hypertension, dyslipidemia, renal insufficiency, cardiac failure, coronary artery disease, arrhythmia (Table 2).

Table 1. Treatment options and outcome of graft limb occlusions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients with occluded limb(s) ($n = 33$) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular</td>
<td>9 (27.2)</td>
</tr>
<tr>
<td>Thrombectomy + stent</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Thrombolysis + stent</td>
<td>6 (18.2)*</td>
</tr>
<tr>
<td>Surgery</td>
<td>22 (66.7)</td>
</tr>
<tr>
<td>Femorofemoral bypass</td>
<td>19 (57.6)</td>
</tr>
<tr>
<td>Axillofemoral bypass</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Conservative</td>
<td>2 (6.1)</td>
</tr>
</tbody>
</table>

* Three bilateral thrombolysis and stenting for bilateral graft limb occlusion.

Table 2. Variables investigated for association with graft limb thrombosis

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Patients with graft limb occlusion ($n = 33$)</th>
<th>Patients with patent graft ($n = 427$)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean +/- SD)</td>
<td>68.5 +/- 8</td>
<td>72.6 +/- 9</td>
<td>.007</td>
</tr>
<tr>
<td>Male</td>
<td>31 (94%)</td>
<td>404 (95%)</td>
<td>.70</td>
</tr>
<tr>
<td>Current smoking</td>
<td>17 (51%)</td>
<td>178 (42%)</td>
<td>.29</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (67%)</td>
<td>226 (53%)</td>
<td>.14</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>11 (33%)</td>
<td>117 (28%)</td>
<td>.48</td>
</tr>
<tr>
<td>Coronary disease</td>
<td>13 (39%)</td>
<td>185 (46%)*</td>
<td>.45</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>10 (30%)</td>
<td>98 (24%)**</td>
<td>.28</td>
</tr>
<tr>
<td>Arhythmia</td>
<td>4 (12%)</td>
<td>64 (15%)</td>
<td>.80</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2 (6%)</td>
<td>48 (1%)</td>
<td>.56</td>
</tr>
</tbody>
</table>

* Data missing for 26 patients.
** Data missing for 13 patients.
Aneurysm’s related factors
Statistical analysis failed to show any significant association with clinical presentation of the aneurysm (symptomatic or asymptomatic), existence of thrombus in the infra renal neck, maximal transverse diameter of the aneurysm, diameter of the infra-renal neck and iliac anatomy pattern (Tables 3 and 4).

Devices and graft configuration
Limb occlusions occurred with any type of stent-grafts (Vanguard, EVT, Stentor, Stenford, Gore, Zenith, and Talent) except for the AneurX device (Table 5). The rate of limb thrombosis was higher with the first generation devices. Seventeen patients out of 91 (18.7%) with a first generation device (EVT, Vanguard, Stentor, Stenford) had limb thrombosis. Conversely, only 16 of 369 patients (4.3%) treated with currently available stent-grafts (Talent, AneurX, Gore, Zenith) occluded their grafts (P < .001). The highest rates of limb occlusion were observed with the EVT graft (4/14, 28.6%) and Stenford device (3/9, 33.3%).

Graft migration, kink and outflow
Graft migration as defined above was recognized in 9 patients (33%) treated with currently available stent-grafts (Talent, AneurX, Gore, Zenith) except for the AneurX device (Table 5). The highest rates of limb occlusion were observed with the EVT graft (4/14, 28.6%) and Stenford device (3/9, 33.3%).

Table 3. Aneurysm related factors investigated for association with graft limb thrombosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with graft occlusion (n = 33)</th>
<th>Patients with patent graft (n = 427)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms n (%)</td>
<td>0</td>
<td>33 (8)</td>
<td>.15</td>
</tr>
<tr>
<td>Thrombus in the infrarenal neck: n (%)</td>
<td>24 (73)</td>
<td>324 (76)</td>
<td>.68</td>
</tr>
<tr>
<td>Maximal transverse diameter (cm) mean +/- SD</td>
<td>54.6 +/- 10</td>
<td>56.5 +/- 13</td>
<td>.33</td>
</tr>
<tr>
<td>Diameter of the infra renal neck (cm) mean +/- SD</td>
<td>22.5 +/- 3</td>
<td>22.9 +/- 4</td>
<td>.40</td>
</tr>
<tr>
<td>Migration of the graft: n (%)</td>
<td>1 (3)</td>
<td>8 (2)</td>
<td>.49</td>
</tr>
</tbody>
</table>

SD, standard deviation.

Table 4. Iliac anatomy pattern investigated for association with graft limb thrombosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Occluded limbs (n = 36)</th>
<th>Patent limbs (n = 793)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal iliac artery angulation &gt; 60°: n (%)</td>
<td>8 (23)*</td>
<td>158 (23)**</td>
<td>.91</td>
</tr>
<tr>
<td>EIA* diameter (mean +/- SD)</td>
<td>8.8 +/- 2.1</td>
<td>9.6 +/- 4</td>
<td>.32</td>
</tr>
<tr>
<td>Extension of the graft to the EIA*: n (%)</td>
<td>8 (22)</td>
<td>156 (9)</td>
<td>.70</td>
</tr>
</tbody>
</table>

SD, standard deviation.

* EIA: external iliac artery (mm).
# : Data missing for two patients.
## : Data missing for 98 patients.

underlying femoral or iliac stenosis >70% and in 31 of 822 limbs (3.8%) without ipsi-lateral underlying occlusive disease (p < 0.001).

Additional limb stenting during follow-up
We studied the relationship of additional stenting of the limbs of the stent- grafts during follow-up and the occurrence of occlusion. Redo stenting was performed in 23 limbs, five (16%) occluded later one. In 806 limbs where no redo stenting was performed 31 limbs thrombosed (3.8%) (p = 0.001).

Multivariate analysis using a logistic regression model showed that kinking (odds ratio [OR] 11.9; 95% confidence interval [95% CI] 3.39–42.1; p = 0.0001), younger age ([OR] 1.05; [95% CI] 1.00–1.09; P = 0.034), first generation devices ([OR] 2.87; CI 1.25–6.62; p = 0.017) were independently related to the occurrence of graft limb occlusion. Underlying vascular stenosis could not be tested in this model due to the small number of events.

Discussion
Endovascular repair has been increasingly used worldwide to treat AAA. While long-term durability still remains uncertain, EVAR has many early
advantages which may explain its liberal used in many institutions: decrease in postoperative morbidity, less blood transfusion, shorter hospital stay and better short-term health-related quality of life. Nevertheless, the benefits come at the price of an increased number of graft-related complications and secondary procedures during follow-up. Limb graft occlusion is one of these adverse events.

The rate of lower extremity ischemia after EVAR was 7% in the current series. In previous reports the percentage varied between 2 and 40% depending mostly upon type of grafts and duration of follow-up. The clinical presentation in the current series included approximately 1/3 of patient with acute limb ischemia, while most patients presented with less severe symptoms or were asymptomatic. These findings are in agreement with Maldonado series. In our series, the majority of limb occlusions (70%) occurred during the first 6 months after implantation of the stent-graft and this is again in agreement with previous reports including Ferman’s one. The etiologic factors of such occlusions are important to consider. Our analysis has found four significant predictive factors including young age, type of device, the presence of a kink and underlying stenotic disease.

We have no clear explanation on the role of age which however has been previously identified as a factor of poor outcome in patient with peripheral vascular disease.

The role of the generation of stent graft was underlined in our series. The rate of occlusion with different stent graft is shown in Table 5. This is in agreement with the Eurostar series findings which have shown that currently commercially available stent-grafts had a lower incidence of complications including occlusion than the first generation grafts. Although the majority of graft limb occlusion occurred within the first six months after EVAR which give a strong support of our findings, the relatively small numbers of first generation devices along with a longer follow-up with these devices are limitations of the study.

We failed to find a statistical significance of graft’s configuration (aortouniiliac versus bifurcated grafts) as regard to limb occlusion. Obviously specific indication for graft configuration makes comparison debatable. Aortouniiliac grafts were indicated in the presence of a narrow aortic bifurcation or in patients with a severely diseased iliac artery on one side. In a retrospective study of 173 endovascular AAA repair, Carpenter et al. found 7 graft limb thrombosis. Aortomonilial grafts with femoro-femoral bypass grafts had a trend toward a better patency rate (97% at 18 months) than bifurcated endografts (90% at 18 months) but as in our series, the difference was not statistically significant.

Kink was the predominant factor of occlusion in our series. Graft limb kinking occurred in 14 limbs of 13 patients and was significantly associated with graft limb occlusion. Diagnosis of kink was established on the first month X-Ray postoperatively in 7 cases and more than one year after initial intervention in the other 7 cases. A part from device related problems such as those observed with the unsupported graft, early kinks development is mostly linked to tortuosity in the iliac arteries or blunt angled bifurcation. This angulation may be missed when the control angiogram is performed before the pull out of the stiff wire which straightens the arteries. Since a significant number of patients had early thrombosis due to this phenomenon, it is our current practice to perform routinely completion angiography without stiff wires. Sivamurthy has shown that in a series of Zenith stent graft, patient in whom a bare stent had been placed in the limb of the graft had no occlusion compared to 7.1% in patient without stents. Aneurysm shrinkage in Eurostar database was significantly associated with limb distortions which ultimately increased the risk of occlusion. Although late kink is mostly linked to migration of the graft, more than aneurysm shrinkage, we failed to identify migration as a factor of thrombosis. This may be explained by our policy of aggressive management of any migration before endoleak or occlusion occurs.

Underlying arterial diseases which developed during the follow-up and which were detected by postoperative Duplex scan were found to be a predictive
factor of occlusion. Reduced flow in the limb of the graft due to outflow impairment is probably explanatory. Similarly to kink development such lesions should not be left untreated.

Among all others factors tested in the current series, none of patient general characteristics such as gender, current smoking, hypertension, dyslipidemia, renal insufficiency, cardiac failure, coronary artery disease, and arrhythmia were predictive of occlusion. Other factors such as coagulation disorders have not been reported with stent graft but are known factors of occlusion after open surgery.

Iliac size, angulations and distal extent of the graft may also play a role in the occurrence of thrombosis. Carrocacio identified small limb diameter (14 mm versus 16 mm) and distal extent of the graft to the external iliac artery as significant factors. This later factor was also underlined by Erzurum. We did not find a correlation with limb diameter but there was a trend toward more thrombosis in the group of patient with limbs placed into the external iliac artery. The rate of limb occlusion occurrence was 5.1% when the ipsilateral limb was extended into the external iliac artery and 4.2% when it was not extended into the common iliac artery ($p = 0.7$). Similarly, the population of occluded limbs had a higher mean maximal angulation of iliac arteries (37.6° versus 28.4°, $P = 0.07$). This difference was not statistically significant.

**Treatment options**

In our series, stent-graft limb thrombosis were successfully treated with endovascular or surgical interventions in all patients except one who died following bilateral graft limb thrombosis.

Thrombolysis followed by stenting was used in 6 cases. Reocclusion occurred in two of those cases, necessitating iterative thrombolysis with further stent placement. Thrombolysis has been shown to be an effective modality in restoring patency in thrombosed vascular grafts. The underlying limb stenosis can then be identified and treated with stent placement. Although thrombolysis therapy is an attractive option, it has many drawbacks. This procedure is time-consuming, and may be complicated by leg embolism, haemorrhages and new endoleak due to the lysis of the thrombus in the aneurysm sack. Mechanical thrombolysis devices may have a role in this setting. In 2 previous reports, 9 patients with graft limb thrombosis were successfully treated with mechanical rheolytic thrombectomy.

In our series, combined interventions including surgical thrombectomy and stenting of the occluded limb were successful in three cases. Nevertheless, this treatment has its own drawback such as stent-graft dislodgement, component separation in modular devices and thrombus migration in the controlateral limb and hypogastric artery. Fortunately such adverse events did not occurred in the current series.

As noted in previous studies, extra anatomic bypasses are very effective with patency rates above 90%. In our series, we did not observed any reocclusion among 22 extra anatomic bypasses. Detection and correction of any stenosis in the donor limb is of paramount importance to maintain long term patency. Good imaging and intraoperative pressure measurements at the time of femorofemoral bypass may be helpful. Contrary to thrombolysis which requires refined technical equipment and ICU availability, femoro-femoral bypasses can be safely performed in every vascular centre.

To summarize, the choice between thrombolysis and extra anatomical repair is not obvious. The single death in this series occurred after thrombolysis. Conversely, the single infection occurred in a patient treated with a femoro-femoral graft. Patient’s condition, severity and length of ischemia, and institutional factors should be taken into consideration for a sound choice.

**References**


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